III.D. A one-page description of the proposed experiment in nontechnical language.

Cystic fibrosis (CF) is the most common lethal hereditary disorder of Caucasians in the U.S. The major manifestations are in the lung, with thick, sticky mucus, chronic infections and inflammation. The average life span is approximately 28 years. The disease is caused by inherited abnormalities of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Because of these genetic abnormalities, the cells lining the airways cannot move salt in a normal fashion, causing the mucus abnormalities, infection and inflammation, and consequent progressive damage to the lung. In the context of laboratory studies demonstrating that transfer of the normal CFTR gene to airway cells from individuals with CF will compensate for the abnormalities in the CFTR gene and permit airway cells to function in a normal fashion, this protocol is directed toward using a modified adenovirus to transfer the normal CFTR gene into the cells lining the airways of individual with CF. Following a period of extensive evaluation, a modified adenovirus (one of the causes of the common cold) will be instilled into the nasal passages and airways of individuals with CF. A variety of biologic and clinical parameters will be used to assess safety, biologic efficacy (the ability of the treatment to correct the abnormalities in the cells lining the airways as assessed by laboratory tests), and clinical efficacy (improvement in the clinical status of the patient). Ten patients will be studied, two each at increasing doses of the modified adenovirus. The therapy will be given one time only to each patient in order to assess safety, efficacy and the response of the immune system to this modified adenovirus. At the conclusion of this study, it should be possible to assess whether this strategy of compensating for the genetic abnormalities of CF will be a rationale approach to treating the respiratory manifestations of this disease.